**PATENT** 

Attorney Docket No.: MEDIV2010-4

In re Application of: Epstein et al.

Application No.: 10/618,183

Filed: July 10, 2003

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## In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Upon entry of the present amendment, the claims will stand as follows:F

Please cancel claims 3, and 9-12, without prejudice

Please amend claims 17, 19, 25, 29-32, 39, 40, 42, 43. 45, 47 and 49 as follows:

Claims 1-16 (cancelled)

17. (Currently Amended) A method for enhancing collateral blood vessel formation in heart or limb muscle tissue, said method comprising:

directly injecting into a site of impaired blood flow in heart or limb muscle tissue an effective amount of early attaching cells obtained from autologous bone marrow, which <u>early attaching</u> cells have been transfected <u>in vitro</u> with an adenoviral vector comprising a polynucleotide encoding one or more angiogenic factors selected from hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS).

Claim 18 (Cancelled)

19. (Currently Amended) The method of claim 17, wherein the early attaching cells [[are]]% consist essentially of marrow-derived stromal cells and the transfected cells are directly injected into a site of ischemia in the muscle tissue.

Claims 20-23 (Cancelled)

24. (Previously Presented) The method of claim 47, wherein the period of culturing is from about 3 hours to about 3 days.

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25. (Currently Amended) The method of claim 17, further comprising filtering the bone marrow [prior to] and culturing [[of]] the bone marrow to obtain the early attaching cells.

Claims 26 - 28 (Cancelled)

- 29. (Currently Amended) The method of claim 17, wherein the [[agent]] <u>angiogenic factor</u> is selected from a fibroblast growth factor (FGF), a NOS, and PR39.
- 30. (Currently Amended) The method of claim 17, wherein the [[agent]] <u>angiogenic factor</u> is selected from FGF-1, FGF-2, FGF-4, and FGF-5.
- 31. (Currently Amended) The method of claim 17, wherein the [[agent]] <u>angiogenic factor</u> is selected from inducible NOS and endothelial NOS.
- 32. (Currently Amended) The method of claim 17, wherein the [[agent]] <u>angiogenic factor</u> is PR39.
- 33. (Cancelled)
- 34. (Previously Presented) The method of claim 17, wherein the method enhances collateral blood vessel formation in the heart or leg muscle tissue.

Claims 35 - 38 (Cancelled)

39. (Currently Amended) A therapeutic composition comprising early attaching cells obtained from bone marrow, which cells have been transfected with an adenoviral vector comprising at least one polynucleotide that encodes one or more [[agents]] angiogenic factors selected from

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hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS).

- 40. (Currently Amended) The composition of claim 39, further comprising conditioned medium in which the cells have been grown in culture for a time sufficient to allow expression of containing one or more of the [[agents]] angiogenic factors expressed from the polynucleotides.
- 41. (Original) The composition of claim 39, wherein the polynucleotide further comprises a transcription regulatory region operatively associated with the polynucleotide.
- 42. (Currently Amended) The composition of claim 39, wherein the transfected cells have been stimulated in vitro by exposure to hypoxia.
- (Previously Presented) The composition of claim 39, further comprising an anticoagulant. 43.
- 44. (Cancelled)
- 45. (Currently Amended) The composition of claim 39, wherein the early attaching cells [[are]] consist essentially of marrow-derived stromal cells.
- 46. (Original) The composition of claim 39, wherein the composition is intended to be injected into a patient having ischemic tissue and the early attaching cells are derived from bone marrow obtained from the patient.
- 47. (Currently Amended) The method of claim 17, further comprising, prior to the injecting, culturing the early attaching cells in a culture medium to produce conditioned medium containing one or more of the [[agents]] angiogenic factors expressed from the polynucleotides, and wherein

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the method further comprises injecting <u>a composition comprising</u> the one or more [[agents]] angiogenic factors in the conditioned medium along with the transfected early attaching cells.[[.]]

- 48. (Previously Presented) The method of claim 17, wherein the injecting is at multiple sites in the muscle tissue.
- 49. (Currently Amended) The method of claim[[48]] <u>47</u>, wherein the effective amount is about 0.2 to about 0.5 ml of the composition in each of from about 12 to about 25 sites.